

Hereditary spastic paraplegia

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Hereditary spastic paraplegia is a rare disease, the first mention of it in the literature probably being by Strümpell (1880), after whom the disease is sometimes named. Rhein (1916), gave a summary of all reports up to that date, 90 in all covering 111 families, and Paskind and Stone (1933) also summarized the literature with accounts of another 36 reports from 40 families. Since then about 50 further reports have appeared, covering some 60 families, bringing the total so far to 176 reports of 215 families. Of these the majority have originated in Germany or elsewhere in Europe, but with a substantial number from the Americas.

In Britain, however, reports are rare, the first being by Philip (1886), under the title of primary spastic paralysis. Then Gee (1889), Tooth (1891, two families), Ormerod (1904), Holmes (1905), Jones (1907), and Ogilvie (1908) each reported its occurrence, Gee, Ormerod, and Holmes describing associated amyotrophy. In the discussion following Ogilvie's report to the Royal Society of Medicine, Dr. Guthrie spoke of another family with the disease known to him. The next report was not until 1939 (Bell and Carmichael) and in recent years that of Bickerstaff (1950), describing the largest recorded British family. Garland and Astley (1950) and Dick and Stevenson (1953) have also described families. Manson (1920), Worster-Drought, Greenfield, and McMenemey (1940), and Sutherland (1957) each

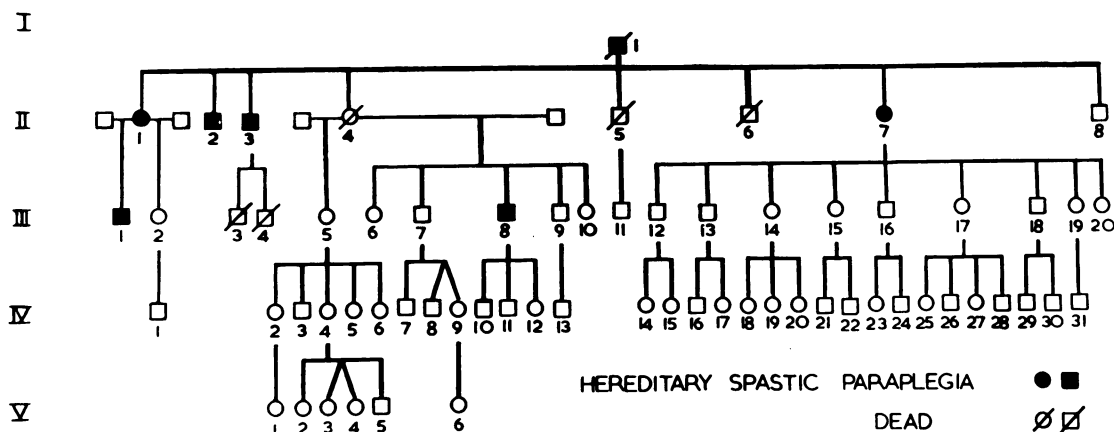
reported similar familial conditions but with the addition of progressive dementia, and therefore they should probably not be included with the foregoing. In this paper yet another family (Fig. 1) is described.

CLINICAL DETAILS

The family studied comprises 66 members over five generations. The eldest member, who died aged 76, was known to have had increasingly stiff legs for at least the last 26 years of his life; II 4 died aged 67 following a stroke; II 5 and II 6 were killed in the First World War; and III 3 and III 4 died in infancy. Information on II 4 was obtained from two independent sources: from one it appeared that she had suffered from 'leg trouble' for which she had received 'electrical treatment', while from the other it was said that she frequently complained of numbness in her legs and often tripped and fell. It is possible that this member also suffered from hereditary spastic paraplegia but the evidence is inadequate.

Of the remaining 60 members, all except two were traced; 47 were examined personally, usually in the subject's own home, and 11 were either not available or were not willing to be examined. Details are given of the six affected members, but for the sake of brevity only abnormal features will be mentioned.

II 1 Emma, aged 78, complained of aches and pains in both legs with occasional leg 'jerking' at night since childhood. The legs had become increasingly stiff and she had had difficulty in walking since the age of 50; she had been bedridden since the age of 69 years. On examination,



muscle tone was markedly increased and power almost nil in the legs. The knee jerks were increased, the ankle jerks unobtainable. Plantar responses were left extensor, right flexor. Marked intention tremor was seen on finger-nose testing. At rest there was a gross 'pill-rolling' tremor of both hands and the lower jaw was tremulous.

II 2 Arthur, aged 75, complained of gradually increasing leg stiffness with frequent tripping since the age of 45 years. He is now unable to stand unaided but can just walk with assistance, and he suffers from frequent painful nocturnal muscle spasms in the legs. On examination, muscle tone was increased in all limbs, particularly the legs. Power was reduced in the trunk and almost nil in the legs, on account of spasticity, which prevented much in the way of even passive movement. Tendon reflexes were increased throughout, especially in the legs. The abdominal reflexes were absent; plantar responses were extensor. There was slight pes cavus and loss of vibration sense below both knees. Slight but definite intention tremor was seen on finger-nose testing.

II 3 Charles, aged 72, complained of gradually increasing leg stiffness since the age of 50 years. On examination, muscle tone was greatly increased and power reduced in the legs. Tendon reflexes were increased throughout, particularly in the legs; abdominal reflexes were absent; plantar responses were extensor. Vibration sense was diminished in both legs and the trunk up to the lower rib margin.

II 7 Louise, aged 64, complained of increasing stiffness and weakness, with shooting pains and recurrent painful nocturnal flexor spasms in both legs, since the age of 62 years. Since that time she had also noticed pins and needles and weakness in both hands and she had occasionally burnt herself without noticing pain. On examination, muscle tone was slightly increased throughout. Power was reduced in the arms, especially in the small muscles of both hands, which showed minimal wasting. Tendon reflexes were increased throughout; abdominal reflexes were absent; plantar responses were extensor. Reduction in sensation to pin prick and temperature below T.1 dermatome was inconstant, with diminution of vibration and position senses in both legs and vibration sense in both hands. Slight intention tremor was seen on finger-nose testing. The gait was stiff and unsteady. A radiograph of the cervical spine showed osteoarthritis of the intervertebral joints in the C.4 to 7 region and a cervical myelogram showed the appearances of posterior disc protrusions at C 3/4 and C 4/5 levels.

III 1 Ernest, aged 50, complained of gradually increasing stiffness of both legs, with frequent tripping, since the age of 43 years. On examination, muscle tone was greatly increased in the legs. Tendon reflexes were increased in the legs, with extensor plantar responses and moderate pes cavus. Slight intention tremor with the right arm was seen on finger-nose testing.

III 8 Albert, aged 45, complained of aching in the right leg at the age of 38, which temporarily improved

but had been progressively worse for the past three years. He frequently caught his right toe and the legs 'jumped' in bed at night. On examination, there was a striking facial resemblance to III 1. Muscle tone was moderately increased in the legs. Tendon reflexes were increased in all limbs and there was slight ankle clonus. The right plantar response was extensor, the left equivocal.

OTHER MEMBERS Examination of the other 41 members seen was wholly normal, with the exception of seven individuals: II 8 had slight horizontal nystagmus; IV 18 had very slight pes cavus; and III 2, III 12, III 13, III 19, and IV 26 had increased tendon reflexes. III 2 also complained that her legs 'jumped' at night. But while reduced reflexes, especially in younger subjects, may excite comment, it is notoriously difficult to assess a slight increase, and in view of the absence of supporting evidence, it would not be permissible to regard any of these seven as even incipient or partial examples of hereditary spastic paraplegia. The 11 individuals who were not examined were all said to be quite normal by near relatives.

'NORMAL' FEATURES OF HEREDITARY SPASTIC PARAPLEGIA

Hereditary spastic paraplegia is rare and necropsy reports rarer. It is thus difficult to establish precisely what are its 'classical' features, and various authorities give different versions. It is true that all agree upon the more common features but there are many accompaniments which are variously included as part of the normal picture or regarded as atypical of it. The principal features are, however, as follows.

AETIOLOGY The condition is familial and is transmitted on a recessive or (less commonly) a dominant basis (Bell and Carmichael, 1939). Sporadic examples are also said to occur (Wilson, 1954). No external cause is known.

AGE OF ONSET AND SEX INCIDENCE The average age of onset in dominant-transmitted stock is 18½ years; in recessive-transmitted stock, 11½ years. Males outnumber females slightly, by about 11 to 10 (Bell and Carmichael, 1939).

PATHOLOGY So far as it is known the pathology seems to vary as much as the clinical features. Thus the basic lesion is a degeneration of the cortico-spinal tracts, which is maximal in the lumbar region. In addition there may be lesions in the posterior columns, optic nerves, cortex, or other parts of the neuraxis, and lesions have also been found at necropsy which have had no clinical counterparts during life. This is especially so with lesions which are not infrequent in the dorsal root ganglia,

despite the fact that sensory disturbance in hereditary spastic paraplegia is minimal or absent and the deep reflexes are invariably preserved.

SYMPTOMS AND SIGNS Stiffness of the legs is usually the first symptom, but the trunk and arms may also be affected later. In young children there may be difficulty in learning to walk. Loss of power is uncommon, although use of the limbs may be limited by stiffness. *Pes cavus* or *equino-varus* often develops, which is subtly different from that found in Friedreich's ataxia. Whereas in hereditary spastic paraplegia the toes are retracted and the foot arched dorsally with shortening antero-posteriorly, the expected high arch on the plantar surface is filled in with soft tissue to produce an almost normal foot-print (Tooth, 1891; Bickerstaff, 1950).

Other features are a scissors gait, uncontrollable knee or ankle clonus, nocturnal flexor spasms of the legs, frequent tripping, and the wearing out of the toes of the shoes. Tendon reflexes in the legs, and sometimes the arms, are at first greatly increased but may become unobtainable later owing to failure of the synergists to relax. Plantar responses are extensor but the abdominal reflexes are generally retained. If the disease starts early in life the legs and the whole pelvic girdle may be underdeveloped, presumably from lack of use, a hypoplasia involving all structures, including bone. There is said to be a strong facial resemblance between affected members of the same family (Bickerstaff, 1950).

There is general agreement on the foregoing positive signs but a wide variety of additional signs has also been described. Although muscle wasting and scoliosis rarely occur, and the absence of sensory, sphincter, cerebellar, extrapyramidal, cranial nerve, or cortical involvement is usually regarded as normal, all these have from time to time been associated, optic atrophy and loss of vibration sense being perhaps the most frequent. The age of onset has also varied widely, from just after birth to beyond 70 years.

Variation in clinical features will present special difficulties in families, such as the one now reported, in which the age of onset is late. Certain neurological abnormalities such as loss of vibration sense in the legs, 'cervical spondylosis', Parkinsonism, or even dementia, are quite frequently found in old age, and these all may be the result merely of degenerative changes rather than of primary disease. One must therefore treat the presence of such signs in older patients with some reserve. It is probable, for example, that the 'pill-rolling' tremor in II 1 is an arteriosclerotic manifestation, however tempting it would be to regard it as an unusual part of the main syndrome.

With all these possible additional physical signs some difficulty arises over the question of definition. There must be reasonable limits to the diagnostic features of a given disorder and in hereditary spastic paraplegia muscle wasting and ataxia present a special problem. Should they be regarded as associated features or does their presence require an alternative diagnosis? Most British and American authors regard the absence of ataxia as an essential and perhaps the sole distinction between hereditary spastic paraplegia and other 'hereditary ataxias', but this criterion is not universally accepted. Many also of the earlier described examples of hereditary spastic paraplegia were considered to be, in fact, examples of chronic motor neurone disease.

Such problems of definition are especially common among the heredo-familial neurological disorders, for each variant cannot be classified as a separate entity, and the field of these disorders is confused by overlapping, often eponymous, syndromes. Certain broad groupings of commonly recurring patterns are, however, essential for nosological convenience, and in the absence of more reliable criteria clinical classification must be made to the nearest established syndrome. On this basis, muscle wasting and even ataxia may be included in hereditary spastic paraplegia, provided that the main feature is a slow, upwardly progressive spastic paresis. On this basis, too, the cases described by Manson (1920), Worster-Drought *et al.* (1940), and Sutherland (1957) should be excluded because of the relatively early onset of dementia which produced an essentially different clinical picture.

Although slight variants of hereditary spastic paraplegia occur, in general the features are consistent within a single family. The course is long, with an expectation of life of about 20 years, although it may be longer in cases starting in adult life, and the patient usually dies from some unrelated illness.

PRESENT FAMILY

The members of the family now reported, with a few exceptions, all live within a few miles of each other near Cambridge. There is no consanguinity. The average age of onset was about 50 years, among the oldest so far described, and the ages of the unaffected members ranged from 1 to 67 years, distributed as follows:—

Unknown	0-10	11-20	21-30	31-40	41-50	51-60	60+
1	21	13	7	6	7	2	2

II 7 (the propositus), had definite radiological evidence of cervical spondylosis and it is accordingly

impossible accurately to apportion the causes of symptoms and signs between this condition and hereditary spastic paraplegia in her case. There does not, however, appear to be any doubt about the diagnosis in the other members. One can only speculate about I 1 and II 4.

Although some affected members had a strikingly similar facial appearance many other unaffected members also had the same family likeness, and no special importance is claimed for this finding. Each affected member had the typical 'progressive paraplegia', but in most there were additional features, and of particular interest were the four individuals who showed intention tremor.

On theoretical and statistical grounds it seems likely that there is an inter-relationship between the purely spastic and the ataxic groups of heredo-familial disorders, but it is noteworthy that Bell and Carmichael (1939) in their wide survey could find no clinical evidence of the two conditions arising in the same stock. They did, however, predict such a possibility, and indeed much earlier Ballet and Rose (1905) and Raymond and Rose (1909) had already described such families. The association of anomalous features in, and intermediate forms between, otherwise clear-cut syndromes raises many interesting speculations regarding the transmission and interrelation of the multitudinous hereditary neurological diseases, and this subject is well discussed elsewhere (Bell and Carmichael, 1939; Roth, 1948; Bickerstaff, 1950). Suffice it to say here that in view of the variety of possible determining factors and our present hazy knowledge of the modes of production of these conditions, the appearance of anomalies and abortive forms need occasion no surprise; indeed the surprising thing is that unequivocal and classical syndromes appear so frequently. In the present family, therefore, the slight ataxia in an otherwise spastic stock provides further evidence for the essential unity of this group of heredo-familial disorders.

SUMMARY

A further British family suffering from hereditary spastic paraplegia is described. In this family there were certainly five, and possibly eight, affected individuals out of a total of 66 members in five generations.

Atypical features were the late age of onset (an average of 48 years) and slight intention tremor in four members.

Seven other individuals were considered to have minor neurological abnormalities which may have represented incipient or abortive forms of the disease.

An outline is given of the variety of clinical features and the difficulties of definition in this condition.

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